REMARKS

The present application is directed to modified viral particles. Claims 1-2, 28-31, and 33-54 are pending. In this Response, Applicants amend Claims 1, 41, 42-44, 48 and 52-54. The amendments do not introduce any new matter.

Priority

On page 2 of the Office Action, the Examiner acknowledges that the currently pending claims have the benefit of priority of U.S. Provisional Patent Application Serial No. 60/390,066, filed June 20, 2002, but asserts that the claims do not have the benefit of priority of the parent U.S. Patent Application Serial No. 10/311,679. Applicants disagree. Applicants assert that the pending claims are entitled to the benefit of priority of the parent U.S. Patent Application Serial No. 10/311,679 based, for example, on the disclosure of immunodeficiency viruses on page 7, lines 19-27, and on page 13, lines 29-30, and on the disclosure of vaccines on page 4, lines 22-25, page 9, lines 28-29, and on pages 27-29. Accordingly, Applicants request that these claims be given the benefit of priority of the parent U.S. Patent Application Serial No. 10/311,679.

Claim Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejects Claims 48 and 52 under 35 U.S.C. §112, first paragraph, as failing to comply with written description requirement. On page 3, top, of the Office Action, the Examiner asserts that the claims contain new matter, a concentration range "0.3% to 2.5%," that is not supported by the application, as filed. In this Response, Applicants amend Claims 48 and 52 to recite the range "0.5 to 2.5%." This range was recited in Claim 48 as previously pending and not rejected by the Examiner. Applicants assert that the claim amendments overcome the rejection and request its withdrawal.

Claim Rejections under 35 U.S.C. §102(b)

The Examiner rejects Claims 1, 2, 28-31 and 33-54 under 35 U.S.C. §102(b) as anticipated by Barrett (U.S. Patent No. 6,136,321), hereinafter "*Barrett.*" In the Response filed September 15, 2006, Applicants argued that *Barrett* fails to teach the reduction in lipid content of the viral particles. On page 5 of the Office Action, second paragraph, the Examiner states that the arguments were not persuasive. The Examiner asserts that the detergent treatment in *Barrett* would lead to the claimed particles, and that the present application, as filed, lists the surfactants as suitable for delipidating the viruses to obtain the claimed particle. *See* pages 5-6 of the Office Action. Applicants request withdrawal of the rejection in view of the claim amendments submitted in this Response and the foregoing arguments.

Applicants amend the claims to recite modified viral particles comprising partially delipidated viral particles either (1) obtained by treating lipid-containing viral particles with an organic solvent that is not a detergent or a surfactant (Claims 1-2, 28-31 and 33-53), or (2) comprising an envelope that does not contain detergent molecules (Claim 54). Support for the amendment is found throughout the specification, for example, on page 16, lines 10-12. In contrast, *Barrett* uses non-ionic surfactants, particularly polysorbate, for inactivating lipid enveloped viruses, and teaches that its inactivated lipid enveloped viruses necessarily contain detergent molecules in their envelope. For at least this reason, *Barrett* does not anticipate the pending claims. In view of the foregoing, applicants assert that *Barrett* fails to anticipate the pending claims, and request that the rejection under 35 U.S.C. 102(b) be withdrawn.

The Examiner asserts on pages 5-6 of the Office Action that the structure of the inactivated viruses in *Barrett* is expected to be the same as Applicants' claimed particles, because Applicants disclose in the specification that detergents/surfactants may be used to delipidate viruses. Applicants bring to the Examiner's attention that Claims 1-2, 28-31 and 33-53 presented in this Response are directed to an embodiment of Applicants' particles that are partially delipidated by an organic solvent that is not a detergent or a surfactant. An

embodiment of a delipidation process that uses detergent/surfactant to reduce lipid content in a viral envelope, even if is discussed in the specification, is not the subject matter of the pending claims. For at least this reason, *Barrett* fails to teach all elements of Claims 1-2, 28-31, and 33-53, and fails to anticipate the claims.

Applicants disagree that one of ordinary skill in the art in the field of the present application would expect that viral particles disclosed in *Barrett*, which are treated with a detergent, would be the same as viral particles partially delipidated with an alcohol. No evidence is provided to support this assertion. Based on the current case law and MPEP 2112, *Barrett* fails to inherently anticipate Applicants' claimed compositions. Under *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999), which is cited in MPEP 2112, in order for a reference to anticipate inherently, extrinsic evidence must clearly show necessary presence of missing descriptive matter. *Barrett* does not teach or suggest any characteristics of Applicants' claimed particles recited in the claims. A simple assertion that the detergent-treated particles in *Barrett* are the same as Applicants' particles is not sufficient to establish that *Barrett* inherently anticipates the claimed composition. Thus, *Barrett* fails to inherently anticipate the currently pending claims for at least this reason.

Modified viral particles partially delipidated by an organic solvent that is not a detergent or a surfactant are structurally different from the viruses in *Barrett* obtained by treatment with non-ionic surfactant. At least one of the differences is that the resulting inactivated viruses in *Barrett* necessarily contain detergent molecules in their envelope. The particles in Claims 1-2, 28-31, and 33-53 are not delipidated by detergents or surfactants and, thus, do not contain detergent or surfactant molecules in their envelopes. *Barrett* therefore fails to inherently or expressly anticipate these claims. Claim 54 expressly recites modified viral particles that do not contain detergent molecules in their envelope. The processes disclosed in *Barrett* do not and cannot result in such particles for the reasons discussed in more detail below. *Barrett* therefore fails to anticipate the pending claims expressly or inherently.

Barrett teaches in column 2, lines 46-49, that, in its detergent-treated vaccines, "the detergent replaces the lipids which normally are connected to the hydrophobic portion of the proteins, whereby a lipid-like environment is created and thus the solubilized proteins are stabilized" (emphasis added). In column 5, lines 38-40, Barrett teaches that "the inactivated virus preparation produced according to the invention contains a stabilizing agent" (emphasis added). The only example of a stabilizing agent that *Barrett* discloses is a detergent, and, in particular, polysorbate at a final concentration of at least 0.05%. *See Barrett*, column 5, lines 31-47, and column 6, lines 1-8.

Although *Barrett* suggests removing a detergent from a viral solution after delipidation by a detergent, *Barrett* fails to teach or suggest removal of the detergent molecules that replaced the lipids from the viral envelope. See *Barrett*, column 5, lines 11-30. Thus, the particles in *Barrett* necessarily contain detergent in place of lipid in their viral envelopes. In contrast, in Applicants' partially delipidated particles, the lipids are simply partially removed from the viral envelope, and no detergent molecules replace them. Thus, based on the disclosure of *Barrett*, one of ordinary skill in the art would expect that viral particles treated with a detergent, as disclosed in *Barrett*, are different from Applicants' partially delipidated viral particles.

Barrett only discusses removal of detergent from "the final product," or inactivated virus-containing solution. *See Barrett*, column 5, line 14. *Barrett* states on lines 28-30 of column 5 that "all the methods ... for removal of non-ionic detergents from a solution are suitable" (emphasis added). Removal of detergent from the solution containing detergent-inactivated viruses, as disclosed in *Barrett*, is different from removal of the detergent molecules that have replaced lipid in the viral envelope of these particles during delipidation. The detergent removal methods that *Barrett* discloses are suitable for reducing concentration of detergent molecules in the solvent phase. However, the detergent molecules entrenched by their hydrophobic interactions with proteins in the envelope of the inactivated particles in *Barrett* are not necessarily removed by these methods. In other words, *Barrett* describes removal of the detergent from the solution, not from the particles.

Barrett fails to teach or suggest removal of detergent from the envelope of inactivated viruses. In fact, removal of the detergent from the envelope of inactivated viruses in *Barrett* would defeat the advantages of the detergent-inactivation procedure disclosed in *Barrett*. Based on *Barrett*, detergent, which replaces the lipids normally connected to the hydrophobic portion of the proteins in the viral particles, is necessary to stabilize the solubilized proteins in the detergent-treated viruses. *See Barrett* column 2, lines 46-49 (also discussed above). Thus, *Barrett* teaches away from removal of detergent from the inactivated viruses and teaches away from the modified viral particles recited in the claims. In order to remain stabilized, the particles in *Barrett* necessarily contain detergent in place of lipid in their viral envelopes. Based on the teaching of *Barrett*, removal of the detergent molecules connected to the hydrophobic portion of the proteins in the inactivated viruses, thereby creating a lipid-like environment stabilizing the envelope proteins, will result in destabilization of the envelope proteins, and thus defeat the advantages of *Barrett*'s detergent-inactivation procedure. Accordingly, *Barrett* does not and cannot teach removal of the detergent molecules from the envelope of its inactivated viruses.

In contrast, in Applicants' partially delipidated particles, the lipids are simply partially removed from the viral envelope, and no detergent molecules replace them. Thus, based on the disclosure of *Barrett*, one of ordinary skill in the art would expect that viral particles treated with a detergent, as disclosed in *Barrett*, are different from Applicants' partially delipidated viral particles. At least one difference is that the particles in *Barrett* contain detergent molecules in the viral envelope after detergent treatment. Applicants' partially delipidated particles, on the other hand, do not contain a detergent in their envelope upon partial delipidation with an organic solvent. Therefore, Applicants' claimed compositions are different from those disclosed by *Barrett*.

Also, the claimed particles are different from those disclosed in *Barrett* at least because *Barrett* explicitly teaches that the parameters of the detergent-based delipidation procedure it uses are adjusted so that "the structural integrity and .... the biological activity of the surface and the enveloping proteins are not affected." *See Barrett*, column 4, lines 46-

49. In contrast, Applicants' organic solvent treatment recited in Claims 1-2, 28-31, and 33-53 results in exposing antigens and/or forcing a structural modification in the viral protein structures. *See* the present application, page 20, lines 11-17; page 21, lines 29-31. Even if an embodiment of a delipidation process that uses detergent/surfactant can also expose antigens and/or force a structural modification in the viral protein structures, it is not the subject matter of the pending claims.

Barrett teaches away from a virus treatment process exposing additional antigens and/or forcing a structural modification in the viral protein structures. *Barrett* teaches, for example, in column 4, lines 46-49, that the structural integrity of the surface and the enveloping proteins in inactivated particles is not affected, and in column 3, lines 16-22, that the structural integrity of the whole virus is largely retained. Thus, in contrast to Applicants' invention, *Barrett* fails to use a process that would expose antigens and/or force a structural modification in the viral protein structures. Therefore, *Barrett* fails to anticipate the claims that recite treatment by an organic solvent for at least this reason.

For at least the foregoing reasons, Applicants assert that *Barrett* fails to anticipate Claims 1, 2, 28-31 and 33-54 under 35 U.S.C. 102(b) and request that claim rejections under 35 U.S.C. 102(b) be withdrawn.

CONCLUSION

The foregoing is submitted as a full and complete response to the Final Office Action mailed December 20, 2006. No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required or credit any overpayment to Deposit Account Number 11-0855.

Applicants assert that the claims are in condition for allowance and respectfully request that the application be passed to issuance. If the Examiner believes that any informalities remain in the case that may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to undersigned agent at (404) 815-3102 or to John K. McDonald at (404) 745-2470 is respectfully solicited.

Respectfully submitted,

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